

Translational Alternative Models and Biomarkers Predictive of Drug or Chemical Cardiovascular Risk

Workshop Agenda

October 10, 2013 (8:00 am–5:20 pm)

- 7:30–8:00 Registration and Poster Setup
- 8:00–8:20 Welcome and Workshop Overview
Warren Casey, PhD, DABT (Host and Workshop Co-Chair)
Acting Director, National Toxicology Program (NTP) Interagency Center for the
Evaluation of Alternative Toxicological Methods (NICEATM)
National Institute of Environmental Health Sciences (NIEHS),
Research Triangle Park, NC
- 8:20–8:30 Health Effects Research to Support the Chemical Safety and Sustainability Program at
EPA’s National Health and Environmental Effects Research Laboratory (NHEERL)
Ronald Hines, PhD, Associate Director for Health
NHEERL, U.S. Environmental Protection Agency (EPA), Research Triangle Park, NC
- 8:30–8:40 NIEHS Perspective on Cardiovascular Risk
Rick Woychik, PhD, Deputy Director
NIEHS, Research Triangle Park, NC
- 8:40–10:30 OPENING SESSION**
- 8:40–8:45 Introduction
Syril Pettit, MEM, Executive Director
Health and Environmental Sciences Institute (HESI), Washington, DC
- 8:45–9:10 Current Cardiovascular Safety Regulatory Testing Guidelines
Jean Wu, MD, PhD, Senior Pharmacologist
Center for Drug Evaluation and Research (CDER)
U.S. Food and Drug Administration (FDA), Silver Spring, MD
- 9:10–9:35 Current Status of Chemical Public Health Risks and Testing Guidelines for Chemical
Cardiovascular Safety Assessments
Kevin Dreher, MS, PhD (Workshop Co-Chair), Principal Investigator
NHEERL, EPA, Research Triangle Park, NC
- 9:35–10:00 Current European Cardiovascular Safety Regulatory Guidelines
Olavi Pelkonen, MD, PhD, Professor of Pharmacology
University of Oulu, Oulu, Finland
- 10:00–10:30 Panel Discussion: Drs. Wu, Dreher, and Pelkonen
Syril Pettit, Moderator
- 10:30–11:00 BREAK — Poster Session

11:00–5:20 SESSION 1 — *In Vitro* Approaches to Assessing Risk of Cardiovascular Toxicity

11:00–11:05 Introduction to Session 1 Part 1

Warren Casey, PhD, DABT, NICEATM

11:05–11:30 Contemporary Pharma Approaches to Cardiac Safety Assessment

Peter Clements, BSc, BVM&S, PhD DipRCPath, MRCVS, FRCPath
Director of Pathology, Safety Assessment Pathology
GlaxoSmithKline, Ware, Hertfordshire, United Kingdom

11:30–11:55 Integrated and Mechanistic Approaches to Cardiac Safety Testing

Norman Stockbridge, MD, PhD, Director
Division of Cardiovascular and Renal Products, Office of New Drugs, CDER
FDA, Silver Spring, MD

11:55–12:20 Cardiac Stem Cells for Chemical Safety Assessment

Mark Mercola, PhD
Professor, University of California, San Diego
Director, Muscle Development and Regeneration Program
Sanford-Burnham Medical Research Institute, La Jolla, California

12:20–1:20 LUNCH

1:20–1:45 Zebrafish as Alternative *In Vivo* Models for Environmental Exposures

David Volz, PhD, Assistant Professor
Department of Environmental Health Sciences, Arnold School of Public Health,
University of South Carolina, Columbia, SC

1:45–2:15 Panel Discussion: Drs. Clements, Stockbridge, Mercola, and Volz

Warren Casey, Moderator

2:15–2:20 Introduction to Session 1 Part 2

Brian Berridge, DVM, PhD, DACVP, Director
Worldwide Animal Research Strategy
GlaxoSmithKline, Research Triangle Park, NC

2:20–2:50 *In Vitro* Assays to Assess Xenobiotic and Drug-Induced Vascular Injury
Using Rat and Cynomolgus Vascular Cell Systems

James Turk, DVM, PhD, DACVP, Pathology Director
Amgen, Thousand Oaks, CA

Brian Wamhoff, PhD, Cofounder and Vice President of Research and Development
HemoShear, Charlottesville, VA

2:50–3:15 Organs-on-Chips for Predicting Pulmonary and Cardiac Toxicity and Efficacy

Anthony Bahinski, PhD, MBA, FAHA, Lead Senior Staff Scientist
Biomimetic Microsystems, Wyss Institute for Biologically Inspired Engineering
Harvard University, Boston, MA

3:15–3:45 BREAK — Poster Session

- 3:45–4:15 Adverse Outcome Pathway for Embryonic Vascular Disruption and Alternative Methods to Identify Chemical Vascular Disruptors
Nicole Kleinstreuer, PhD, Bioinformatics Specialist
Integrated Laboratory Systems (ILS), Inc. (Contractor for NICEATM)
Research Triangle Park, NC
Tamara Tal, PhD, Postdoctoral Fellow
Integrated Systems Toxicology Division, NHEERL
EPA, Research Triangle Park, NC
- 4:15–4:40 Alternative Methods to Predict Cardiac Teratogenic Properties of Chemicals
E. Sidney Hunter, PhD
Integrated Systems Toxicology Division, NHEERL
EPA, Research Triangle Park, NC
- 4:40–5:10 Panel Discussion: Drs. Turk, Wamhoff, Bahinski, Kleinstreuer, Tal, and Hunter
Brian Berridge, Moderator
- 5:10–5:20 Closing Remarks
Warren Casey, PhD, DABT, NICEATM

October 11, 2013 (8:00 am–3:00 pm)

- 8:00–8:05 Opening Remarks
Warren Casey, PhD, DABT, NICEATM
- 8:05–9:55 SESSION 2 — *In Silico* Approaches to Cardiovascular Toxicity Risk**
- 8:05–8:10 Introduction
TBD
- 8:10–8:35 *In Silico* Modeling of Cardiac Function
J. Jeremy Rice, PhD, Research Staff Member
Functional Genomics and Systems Biology Group
IBM, Yorktown Heights, NY
- 8:35–9:00 Computational Toxicology Approaches to Cardiovascular Safety Assessment
Naomi Kruhlak, PhD, Senior Staff Fellow
Division of Cardiovascular and Renal Products, Office of New Drugs, CDER
FDA, Silver Spring, MD
- 9:00–9:25 Physiologic Modeling for Cardiovascular Safety at the FDA
Thomas Colatsky, PhD, Director
Division of Drug Safety Research, Office of Testing and Research
Office of Pharmaceutical Science, CDER
FDA, Silver Spring, MD
- 9:25–9:55 Panel Discussion: Drs. Rice, Kruhlak, and Colatsky
TBD, Moderator
- 9:55–10:25 BREAK — Poster Session
- 10:25–3:25 SESSION 3 — Modeling Sensitive or Susceptible Individuals and Populations**
- 10:25–10:30 Introduction
Thomas Colatsky, PhD, FDA
- 10:30–10:55 Introduction to Patient Susceptibilities and How They Influence Drug and Environmental Liabilities
TBD
- 10:55–11:20 Use of Stem Cells Derived from Patient Populations
Craig T. January, MD, PhD, FACC, Professor of Medicine
Cellular and Molecular Arrhythmia Research Program
Division of Cardiovascular Medicine, School of Medicine and Public Health
University of Wisconsin–Madison, Madison, WI
- 11:20–11:45 Engineered Heart Tissues for Cardiac Safety Studies
Tetsuro Wakatsuki, PhD, Cofounder and Chief Scientist
InvivoSciences, Madison, WI
- 11:45–12:45 LUNCH**
- 12:45–1:10 Heart on a Chip — A Novel Platform for Cardiovascular Preclinical Research

Moran Yadid, PhD, Postdoctoral Fellow
Disease Biophysics Group, Harvard School of Engineering and Applied Sciences
Harvard University, Boston, MA

1:10–1:35 Evidence-Based Approaches to Toxicology Testing

Thomas Hartung, MD, PhD, Director,
Center for Alternatives to Animal Testing, Bloomberg School of Public Health
Johns Hopkins University, Baltimore, MD

1:35–2:05 Panel Discussion: Drs. TBD, January, Wakatsuki, Yadid, and Hartung

Thomas Colatsky, Moderator

2:05–2:15 BREAK

2:15–2:45 Final Discussion: Panel members TBD

2:45–3:00 Closing Remarks and Adjournment

Warren Casey, PhD, DABT, NICEATM